UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/314,698	05/19/1999	STEVEN PERRIN	14791-501(AR	5542

7590 12/10/2001

MINTZ LEVIN COHN FERRIS
GLOVSKY AND POPEO PC
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER
EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1655	18

DATE MAILED: 12/10/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/314,698	PERRIN ET AL.	
	Examiner	Art Unit	
	Juliet C Einsmann	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 9/25/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/314698 is acceptable and a CPA has been established. An action on the CPA follows.

2. The request for a CPA was not accompanied by any amendment or arguments. The arguments presented with the previously entered after final amendment (paper number 10) are addressed after the reiterated statements of rejections.

Claim Rejections - 35 USC § 103

3. Claims 1-10, 12-14, 21, 25 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kayne et al. (WO 9843088) in view of Gress *et al.* (Mammalian Genome 3: 609-612, 1992).

Kayne et al. teach a method for identifying and isolating non-redundant nucleic acid fragments which comprises the steps of: providing a library containing undefined nucleic acid sequences (p. 2, lines 9-10), hybridizing said library to a collection of defined nucleic acid sequences (p. 2, line 8), wherein the defined nucleic acid sequences have been previously sequenced and/or are of known origin (p. 3, line 17-18), recovering non-hybridized nucleic acid sequences (p. 2, lines 10-11), and sequencing the non-hybridized nucleic acid sequences (see abstract and p. 9, lines 9-10). In the method taught by Kayne et al., the collection of defined nucleic acid sequences is bound to a surface (p.2, line 8), wherein the surface may be an array (p. 5, line 31), and the preferred surface for such and array is glass (p. 6, line 12). The method

teaches that the sequences to be hybridized to the array should be labeled to permit detection of the DNA which hybridizes to the immobilized sequences (p. 7, line 16-17).

With respect to claims 2-7, 14, and 17, Kayne et al. teach the library of unknown fragments can include gene or gene fragments, may be a random cDNA library, may be genes from an organ, or may be set of RNAs (p. 6, lines 26-28). With respect to claims 8-9, and step (a) of claims 11-14, Kayne teach that a library may also contain PCR products from genomic libraries (p. 4, line 2). With respect to claim 10, Kayne teaches that the label used can be fluorescence, radioactivity, photoactiviation, biotinylation, energy transfer or the like (p. 7, lines 17-19). With respect to claim 13, in the method of Kayne et al., nucleic acids on a grid are exposed to a library containing undefined nucleic acid sequences, and this library is considered to be a set of pooled labeled probes (p. 2, lines 9-10).

The method of Kayne et al. differs from the claimed method because in the method of Kayne et al. the collection of defined nucleic acid sequences is bound to a surface, and in the claimed method the undefined nucleic acid sequences are bound a microarray. Gress et al. teach a method for hybridization fingerprinting of high-density cDNA-library arrays with cDNA pools in which a random cDNA library is hybridized to a micorarray with the help of a robotic device (p. 609). Gress et al. teach that the spotting cDNAs onto a microarray allows for the screening of thousands of clones at one time, and also provides a method which is adaptable for automated analysis.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Kayne et al. so as to have spotted the library

of random nucleic acids on the microarray in order to have provided an improved method for isolating and identifying non-redundant nucleic acids since concerning large scale DNA characterization projects Gress et al. state, "As we have shown in our work with genomic libraries, such large-scale projects can most easily be performed with library arrays spotted at high clone density with a robotic device..." (p. 613).

With respect to claims 11-14 Kayne in view of Gress do not explicitly teach step (f) of the instantly claimed invention, which comprises repeating the hybridization, detection, and identification of the probes which did not hybridize in order to identify additional sequences. However, this step would also have been obvious to a practitioner of ordinary skill in the art for the reasons that follow. Kayne et al. do teach that in some cases it is desired to repeat some steps in the method to control the size and content of the resulting subtraction library (p. 8, lines 7-9), and they specifically teach that "it is preferred that multiple rounds of hybridization are carried out" (p. 8, line 13). Considering this teaching of Payne et al., it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have repeated any of the steps in the method for the added benefit of increasing the amount of sequences detected. Further, "selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results" (MPEP 2144.04). In the instant case, applicant is simply choosing to repeat already disclosed steps, and this would have been obvious to one of ordinary skill in the art. With respect to claim 25, when such repetition it would have been further *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included a probe that recognized the most recently sequenced nucleic acid when the steps

were repeated since the methods of Kayne *et al.* are specifically designed to identify unknown sequences.

Finally, the examiner notes that these claims have different preambles, but substantially the same method steps, and a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. In the case of these claims, the preamble was only directed to the purpose of the process, the steps could stand alone and did not depend on the preamble for completeness, and therefore, the different preambles were not given strong consideration in analysis of the claims (see MPEP 2111.02).

4. Claims 15-17 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al (US Patent 5690894) in view of Schena *et al.* (Science (1995) 270:467-470).

Pinkel et al. disclose a method for enrichment and/or isolation of DNA sequences that are unique to a population which comprises the steps of: amplifying random samples of nucleic acid fragments, such as by using Alu or degenerate oligonucleotide primers in a PCR reaction (Col. 16, lines 64-65), immobilizing the amplification products as an array to form a biosensor (Col. 17, lines 7-14), exposing the biosensor to labeled nucleic acid probes from two sources (Col. 15, lines 40-47) wherein the labeled nucleic acids can be derived from genomic samples (Col. 16, lines 37-40) or from mRNA (Col. 16, lines 44-45), detecting hybridization of nucleic acids from the first and second source (Col. 15, lines 60-65), and then determining the identity of the

hybridized molecules using clones which have been previously mapped which is an analytical approach for determining the identity of the nucleic acid fragment (Col. 17, lines 46-54). Pinkel et al. teach that this method can be used to detect sequences which are under-represented in a sample or over-represented in a sample by comparing the strength of the hybridization signals from the two nucleic acid populations (Col. 15, lines 18-23).

Pinkel *et al.* do not teach methods in which the random samples of nucleic acid fragments are immobilized on a coated glass surface.

Schena *et al.* teach methods for monitoring gene expression patterns using a microarray spotted onto a glass microscope slide (p. 467). Schena *et al.* further teach the use of two-color hybridization experiments on the microarray (469). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have spotted the random nucleic acid fragments taught by Pinkel *et al.* onto a glass slide as taught by Schena *et al.* The ordinary practitioner would have been motivated to have made such a substitution in order to create a high capacity system for monitoring the presence of genes since Schena *et al.* teach that " because of the small format and high density of the arrays, hybridization volumes of 2 microliters could be used that enabled detection of rare transcripts in probe mixtures derived from 2 micrograms of total cellular messenger RNA."

5. Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pinkel et al. in view of Schena *et al.* in view of Maslyn et al.

Pinkel et al. teach a method for discovery of DNA sequences which comprises the steps of: amplifying random samples of nucleic acid fragments, such as by using Alu or degenerate

oligonucleotide primers in a PCR reaction (Col. 16, lines 64-65), immobilizing the amplification products as an array to form a biosensor (Col. 17, lines 7-14), hybridizing labeled probes to the biosensor (Col. 15, lines 40-47) wherein the labeled nucleic acids can be derived from genomic samples (Col. 16, lines 37-40) or from mRNA (Col. 16, lines 44-45), detecting hybridization of the labeled probes to the biosensor (Col. 15, lines 60-65), and then determining the identity of the hybridized molecules using clones which have been previously mapped which is an analytical approach for determining the identity of the nucleic acid fragment (Col. 17, lines 46-54). Pinkel et al. teach that this method can be used to detect sequences which are under-represented in a sample or over-represented in a sample by comparing the strength of the hybridization signals from the two nucleic acid populations (Col. 15, lines 18-23), and Pinkel specifically teaches that some hybridization signals will be stronger than others, and it is a necessary fact that if some hybridization signals are stronger there must also be weaker signals. Stringency is an routinely optimizable parameter and Pinkel teaches that standard techniques for hybridization are to be used (Col. 20, lines 1-2).

Pinkel *et al.* do not teach methods in which the random samples of nucleic acid fragments are immobilized on a coated glass surface.

Schena *et al.* teach methods for monitoring gene expression patterns using a microarray spotted onto a glass microscope slide (p. 467). Schena *et al.* further teach the use of two-color hybridization experiments on the microarray (469). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have spotted the random nucleic acid fragments taught by Pinkel *et al.* onto a glass slide as taught by Schena *et al.* The

ordinary practitioner would have been motivated to have made such a substitution in order to create a high capacity system for monitoring the presence of genes since Schena *et al.* teach that " because of the small format and high density of the arrays, hybridization volumes of 2 microliters could be used that enabled detection of rare transcripts in probe mixtures derived from 2 micrograms of total cellular messenger RNA."

Neither Pinkel *et al.* not Schena *et al.* teach a step in which the obtained DNA sequences are compared to other DNA sequences.

Maslyn et al. teach that a "cluster" is a group of clones related to one another by sequence homology (Col. 7, lines 43-44), and that determining a cluster is achieved by comparing the sequence of against a library or database of sequences (Col. 12, lines 12-16).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included the comparison step of Maslyan et al. in the method taught by Pinkel et al. Maslyn specifically teaches that this is a useful method "to look for homologous, and presumably functionally related sequences in other tissues or samples." This is particularly useful in the context of method of Pinkel et al. since Pinkel et al. expressly compares two different cell types and is interested in the relationship between the cell types (Col. 15).

Response to applicant's remarks

Rejections over Kayne *et al.* in view of Gress *et al.* (claims 1-10, 12-14, 21, and 26)

The fundamental difference between the method of Kayne *et al.* in the instantly claimed method is that in the methods of Kayne *et al.* undefined sequences are in solution and the

defined nucleic acid sequences are bound to a solid support. Beyond that difference, the teachings of Kayne *et al.* meet all of the limitations of the instant claims as discussed in the rejections in paper number 8. Gress *et al.* clearly provide the teaching and motivation for changing the method of Kayne *et al.* so as to anchor the undefined sequences in the method taught by Kayne *et al.* onto a solid support, as Gress *et al.* specifically teach that methods which employ such a step allow for the screening of thousands of clones simultaneously as well as the possibility of automation.

Applicant argues at page three that Gress *et al.* lack any motivation for substituting hybridization with an undefined sequence as taught by Kayne with a probe corresponding to previously arrayed or sequence fragments. However, this Kayne *et al.* specifically teach the use of probes corresponding to previously arrayed or sequenced fragments (p. 2, line 8 of Kayne *et al.*) and therefore, does not need to be provided by Gress *et al.* As discussed above, Gress *et al.* is relied upon merely for the suggestion modify the teaching of Kayne *et al.* so that the undefined sequences are bound to a solid support. Upon this modification of the method of Kayne *et al.* the ordinary practitioner would have therefore used the labeled probes taught by Kayne *et al.* in solution.

Applicant further argues at page four that the rejection over Kayne *et al.* in view of Gress *et al.* do not meet the limitation of claims 21 and 26 which require identifying at least one immobilized fragment that hybridizes weakly or does not hybridize to a labeled probe. However, Kayne *et al.* specifically teach the identification of non-hybridized nucleic acid sequences (see abstract and p. 9, lines 9-10). When the teachings of Kayne *et al.* are modified in view of the

teachings of Gress *et al.* (as discussed above) these non-hybridized sequences would indeed be immobilized.

Applicant argues that the teachings of Kayne *et al.* and Gress *et al.* do not teach repeating the steps of the instant invention, as required by claims 12-14 and 26. However, Kayne et al. do teach that in some cases it is desired to repeat some steps in the method to control the size and content of the resulting subtraction library (p. 8, lines 7-9), and they specifically teach that "it is preferred that multiple rounds of hybridization are carried out" (p. 8, line 13). Considering this teaching of Kayne et al., it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have repeated any of the steps in the method for the added benefit of increasing the amount of sequences detected. Further, "selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results" (MPEP 2144.04). In the instant case, applicant is simply choosing to repeat already disclosed steps, and this would have been obvious to one of ordinary skill in the art.

Rejection over Pinkel *et al.* in view of Schena *et al.*

Applicant argues that the placing a coated glass surface on an optical fiber array would result the blocking of transmission of light through the optical fibers. However, the rejection does not suggest placing a glass surface on an optical fiber, instead the rejection suggests substituting the glass surface for the optical fiber array. The rejection provides motivation for such a substitution from the teachings of Schena *et al.* as discussed in the rejection above.

Conclusion

6. No claims are allowed.

7. This is a CPA of applicant's earlier Application No. 09314698. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

8. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C. Einsmann
Examiner
Art Unit 1655

December 4, 2001